

PCT

WORLD INTELLECTUAL PROPERTY ORGANIZATION  
International Bureau



INTERNATIONAL APPLICATION PUBLISHED UNDER THE PATENT COOPERATION TREATY (PCT)

<b>(51) International Patent Classification<sup>6</sup> :</b> C12N 15/87, 15/62, 15/10, A61K 48/00 // C07K 14/28, 14/24		<b>A3</b>	<b>(11) International Publication Number:</b> WO 99/41402
			<b>(43) International Publication Date:</b> 19 August 1999 (19.08.99)
<b>(21) International Application Number:</b> PCT/US99/03023			<b>(81) Designated States:</b> AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, UZ, VN, YU, ZW, ARIPO patent (GH, GM, KE, LS, MW, SD, SZ, UG, ZW), Eurasian patent (AM, AZ, BY, KG, KZ, MD, RU, TJ, TM), European patent (AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE), OAPI patent (BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG).
<b>(22) International Filing Date:</b> 10 February 1999 (10.02.99)			
<b>(30) Priority Data:</b> 09/021,769 11 February 1998 (11.02.98) US 60/074,294 11 February 1998 (11.02.98) US			
<b>(71) Applicant:</b> MAXYGEN, INC. [US/US]; 3410 Central Expressway, Santa Clara, CA 95051 (US).			
<b>(72) Inventors:</b> PUNNONEN, Juha; 4290 Wilkie Way #P, Palo Alto, CA 94306 (US). STEMMER, Willem, P., C.; 108 Kathy Court, Los Gatos, CA 95030 (US). HOWARD, Russell; 12700 Viscayno Road, Los Altos Hills, CA 94022 (US). PATTEN, Phillip, A.; 261 La Cuesta Drive, Menlo Park, CA 94028 (US).			
<b>(74) Agents:</b> SMITH, Timothy, L. et al.; Townsend and Townsend and Crew LLP, 8th floor, Two Embarcadero Center, San Francisco, CA 94111-3834 (US).			<b>(88) Date of publication of the international search report:</b> 11 November 1999 (11.11.99)
<b>(54) Title:</b> TARGETING OF GENETIC VACCINE VECTORS			
<b>(57) Abstract</b>  This invention provides methods of obtaining reagents for increasing the specificity of genetic vaccines for a desired target cell or tissue type. The invention also provides delivery vehicles for use to improve genetic vaccine specificity for a target cell or tissue type.			

**FOR THE PURPOSES OF INFORMATION ONLY**

Codes used to identify States party to the PCT on the front pages of pamphlets publishing international applications under the PCT.

AL	Albania	ES	Spain	LS	Lesotho	SI	Slovenia
AM	Armenia	FI	Finland	LT	Lithuania	SK	Slovakia
AT	Austria	FR	France	LU	Luxembourg	SN	Senegal
AU	Australia	GA	Gabon	LV	Latvia	SZ	Swaziland
AZ	Azerbaijan	GB	United Kingdom	MC	Monaco	TD	Chad
BA	Bosnia and Herzegovina	GE	Georgia	MD	Republic of Moldova	TG	Togo
BB	Barbados	GH	Ghana	MG	Madagascar	TJ	Tajikistan
BE	Belgium	GN	Guinea	MK	The former Yugoslav Republic of Macedonia	TM	Turkmenistan
BF	Burkina Faso	GR	Greece	ML	Mali	TR	Turkey
BG	Bulgaria	HU	Hungary	MN	Mongolia	TT	Trinidad and Tobago
BJ	Benin	IE	Ireland	MR	Mauritania	UA	Ukraine
BR	Brazil	IL	Israel	MW	Malawi	UG	Uganda
BY	Belarus	IS	Iceland	MX	Mexico	US	United States of America
CA	Canada	IT	Italy	NE	Niger	UZ	Uzbekistan
CF	Central African Republic	JP	Japan	NL	Netherlands	VN	Viet Nam
CG	Congo	KE	Kenya	NO	Norway	YU	Yugoslavia
CH	Switzerland	KG	Kyrgyzstan	NZ	New Zealand	ZW	Zimbabwe
CI	Côte d'Ivoire	KP	Democratic People's Republic of Korea	PL	Poland		
CM	Cameroon	KR	Republic of Korea	PT	Portugal		
CN	China	KZ	Kazakstan	RO	Romania		
CU	Cuba	LC	Saint Lucia	RU	Russian Federation		
CZ	Czech Republic	LI	Liechtenstein	SD	Sudan		
DE	Germany	LK	Sri Lanka	SE	Sweden		
DK	Denmark	LR	Liberia	SG	Singapore		
EE	Estonia						

# INTERNATIONAL SEARCH REPORT

International Application No  
PCT/US 99/03023

## A. CLASSIFICATION OF SUBJECT MATTER

IPC 6 C12N15/87 C12N15/62 C12N15/10 A61K48/00 //C07K14/28,  
C07K14/24

According to International Patent Classification (IPC) or to both national classification and IPC

## B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)

IPC 6 C12N C07K A61K

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practical, search terms used)

## C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	WO 97 20078 A (AFFYMAX TECH NV ;CRAMER I ANDREAS (US); STEMMER WILLEM P C (US)) 5 June 1997 (1997-06-05) abstract page 6, line 20 - page 9, line 9 page 58, line 3 - page 59, line 10 claim 1	1-50
A	WO 94 25608 A (BAYLOR COLLEGE MEDICINE) 10 November 1994 (1994-11-10) abstract page 5, line 28 - line 30 page 7, line 1 - line 19 examples 1-12 claims 1-19 figures 1-4	1-17

☒ Further documents are listed in the continuation of box C.

☒ Patent family members are listed in annex.

### \* Special categories of cited documents :

- "A" document defining the general state of the art which is not considered to be of particular relevance
- "E" earlier document but published on or after the international filing date
- "L" document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)
- "O" document referring to an oral disclosure, use, exhibition or other means
- "P" document published prior to the international filing date but later than the priority date claimed

- "T" later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention
- "X" document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone
- "Y" document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art.
- "&" document member of the same patent family

Date of the actual completion of the international search

10 September 1999

Date of mailing of the international search report

22.09.1999

Name and mailing address of the ISA

European Patent Office, P.B. 5818 Patentlaan 2  
NL - 2280 HV Rijswijk  
Tel. (+31-70) 340-2040, Tx. 31 651 epo nl.  
Fax: (+31-70) 340-3016

Authorized officer

Galli, I

## INTERNATIONAL SEARCH REPORT

International Application No  
PCT/US 99/03023

C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT		
Category	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
A	WO 91 07979 A (INNOVATIVE TECH CENTER) 13 June 1991 (1991-06-13) abstract claims 1-19 ---	18-23
A	EP 0 125 228 A (HARVARD COLLEGE) 14 November 1984 (1984-11-14) abstract ---	21
A	WO 94 23738 A (MEDISORB TECHNOLOGIES INTERNAT) 27 October 1994 (1994-10-27) abstract claims 1-9 ---	24-45
A	WO 95 16027 A (BIOINVENT INT AB ;BORREBAECK CARL A K (SE); DUENAS MARTA (CU)) 15 June 1995 (1995-06-15) abstract figure 1 claims 1-5 ---	24-45
A	WO 94 26787 A (UNIV LELAND STANFORD JUNIOR) 24 November 1994 (1994-11-24) abstract figures 1,2 claims 1-14 ---	24-45
A	WO 97 11605 A (DANA FARBER CANCER INST INC ;UNIV PITTSBURGH (US)) 3 April 1997 (1997-04-03) abstract ---	24-45
A	WO 96 13250 A (AMGEM INC) 9 May 1996 (1996-05-09) abstract page 1 - page 5 examples 1-3 claims 1-23 ---	46-50
A	WO 96 23882 A (UNIV ROCKEFELLER ;STEINMAN RALPH M (US); NUSSENZWEIG MICHEL C (US)) 8 August 1996 (1996-08-08) abstract page 3, line 1 - page 4, line 7 claims 28-32 ---	1-50
A	WO 97 35957 A (MAXYGEN INC ;STEMMER WILLEM P C (US)) 2 October 1997 (1997-10-02) abstract page 5, line 5 - line 30 claims 32-41 ---	1-50
-/--		

# INTERNATIONAL SEARCH REPORT

Inter      nal Application No  
PCT/US 99/03023

C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT		
Category	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
A	<p>PATTEN P A ET AL: "APPLICATIONS OF DNA SHUFFLING TO PHARMACEUTICALS AND VACCINES" CURRENT OPINION IN BIOTECHNOLOGY, vol. 8, 1997, pages 724-733, XP002916609 the whole document</p> <p>-----</p>	1-50

# INTERNATIONAL SEARCH REPORT

International application No.  
PCT/US 99/03023

## Box I Observations where certain claims were found unsearchable (Continuation of Item 1 of first sheet)

This International Search Report has not been established in respect of certain claims under Article 17(2)(a) for the following reasons:

1. ☐ Claims Nos.:  
because they relate to subject matter not required to be searched by this Authority, namely:
2. ☐ Claims Nos.:  
because they relate to parts of the International Application that do not comply with the prescribed requirements to such an extent that no meaningful International Search can be carried out, specifically:
3. ☐ Claims Nos.:  
because they are dependent claims and are not drafted in accordance with the second and third sentences of Rule 6.4(a).

## Box II Observations where unity of invention is lacking (Continuation of Item 2 of first sheet)

This International Searching Authority found multiple inventions in this international application, as follows:

see additional sheet

1. ☒ As all required additional search fees were timely paid by the applicant, this International Search Report covers all searchable claims.
2. ☐ As all searchable claims could be searched without effort justifying an additional fee, this Authority did not invite payment of any additional fee.
3. ☐ As only some of the required additional search fees were timely paid by the applicant, this International Search Report covers only those claims for which fees were paid, specifically claims Nos.:
4. ☐ No required additional search fees were timely paid by the applicant. Consequently, this International Search Report is restricted to the invention first mentioned in the claims; it is covered by claims Nos.:

Remark on Protest

☐ The additional search fees were accompanied by the applicant's protest.

☒ No protest accompanied the payment of additional search fees.

FURTHER INFORMATION CONTINUED FROM PCT/SA/ 210

This International Searching Authority found multiple (groups of) inventions in this international application, as follows:

1. Claims: (1-17) - complete

A method for obtaining a binding molecule useful for increasing the uptake or specificity of a genetic vaccine to a target cell, the method comprising:

creating a library of recombinant polynucleotides by recombining (i) nucleic acids that encodes a polypeptide comprising a nucleic acid binding domain, and (ii) nucleic acids that encode a polypeptide comprising a cell-specific binding domain; and

screening the library for a molecule that can bind to a nucleic acid and to a cell-specific receptor.

2. Claims: (18-23) - complete

A method for obtaining an optimized cell-specific binding moiety useful for increasing uptake, efficacy or specificity of a genetic vaccine for a target cell.

Said method, involving recombination of different polynucleotides encoding a receptor-binding moiety of V. cholerae CT-B enterotoxin.

3. Claims: (24-45) - complete

A method of obtaining a genetic vaccine component that confers upon a vector an enhanced ability to enter an antigen-presenting cell, the method comprising:

creating a library of recombinant nucleic acids by subjecting to recombination at least two forms of a polynucleotide,

contacting a library of vectors, each of which comprises a member of the library of nucleic acids created above, with a population of antigen-presenting or antigen-processing cells,

and determining the percentage of the cells that contain the vector.

4. Claims: (46-50) - complete

Idem as subject matter 2, but involving recombination of different polynucleotides encoding bacterial invasin.

## INTERNATIONAL SEARCH REPORT

Information on patent family members

International Application No

PCT/US 99/03023

Patent document cited in search report		Publication date	Patent family member(s)	Publication date
WO 9720078	A	05-06-1997	US 5811238 A AU 1087397 A AU 2542697 A CA 2239099 A EP 0876509 A EP 0906418 A EP 0911396 A WO 9735966 A US 5837458 A	22-09-1998 19-06-1997 17-10-1997 05-06-1997 11-11-1998 07-04-1999 28-04-1999 02-10-1997 17-11-1998
WO 9425608	A	10-11-1994	AU 6713894 A SG 54115 A	21-11-1994 16-11-1998
WO 9107979	A	13-06-1991	CA 2069106 A EP 0502099 A JP 5503420 T	30-05-1991 09-09-1992 10-06-1993
EP 0125228	A	14-11-1984	US 4882278 A AT 35152 T AU 585481 B AU 2727084 A CA 1326218 A DE 3472114 A DK 213784 A EG 17879 A GR 81986 A IE 57266 B JP 2012452 C JP 7040921 B JP 60037980 A PH 25301 A PT 78478 A, B YU 76384 A ZM 2884 A ZW 6884 A	21-11-1989 15-07-1988 22-06-1989 01-11-1984 18-01-1994 21-07-1988 30-10-1984 30-08-1991 12-12-1984 01-07-1992 02-02-1996 10-05-1995 27-02-1985 30-04-1991 01-05-1984 31-08-1989 22-04-1985 19-09-1984
WO 9423738	A	27-10-1994	AU 6707194 A CA 2160878 A EP 0696200 A JP 8510639 T NZ 265818 A	08-11-1994 27-10-1994 14-02-1996 12-11-1996 22-09-1997
WO 9516027	A	15-06-1995	AT 178092 T AU 686292 B AU 1252195 A CA 2178205 A DE 69417446 D DE 69417446 T EP 0739413 A JP 9506000 T US 5712089 A	15-04-1999 05-02-1998 27-06-1995 15-06-1995 29-04-1999 02-09-1999 30-10-1996 17-06-1997 27-01-1998
WO 9426787	A	24-11-1994	NONE	
WO 9711605	A	03-04-1997	AU 7251596 A BG 102355 A CA 2233278 A CN 1201369 A	17-04-1997 30-04-1999 03-04-1997 09-12-1998



# INTERNATIONAL SEARCH REPORT

Information on patent family members

Inter national Application No

PCT/US 99/03023

Patent document cited in search report	Publication date	Patent family member(s)	Publication date
WO 9711605 A		CZ 9800929 A	16-09-1998
		EP 0863704 A	16-09-1998
		HU 9802651 A	01-02-1999
		NO 981386 A	28-05-1998
		NZ 319891 A	28-01-1999
		PL 325953 A	17-08-1998
		SK 40198 A	04-11-1998
WO 9613250 A	09-05-1996	AU 4010395 A	23-05-1996
WO 9623882 A	08-08-1996	AU 4970296 A	21-08-1996
		CA 2211993 A	08-08-1996
		EP 0808366 A	26-11-1997
		JP 10513350 T	22-12-1998
WO 9735957 A	02-10-1997	AU 2337797 A	17-10-1997
		EP 0932670 A	04-08-1999
		AU 2542697 A	17-10-1997
		EP 0906418 A	07-04-1999
		WO 9735966 A	02-10-1997
		US 5837458 A	17-11-1998